

(a) applying said sample to a deposited continuous thin film by either adsorption or directly to a surface of said deposited continuous thin film, wherein said deposited thin film is selected from the group consisting of: semiconductors, insulators, and any combinations thereof; and

(b) analyzing said sample by light desorption-/ionization mass spectroscopy.

REMARKS

Attached hereto is a marked-up version of the changes made to the claims by the current amendment. The attached pages are captioned "**Version with Markings to Show Changes Made.**"

Claims 1-3, 6, 7, 10-12, 14-19, 66, 67, 69 and 70 are currently pending and are now under examination.

Claim 1 has been amended for purposes of clarification of the invention. It is respectfully submitted that the amendment of this claim is neither narrowing nor made for substantial reasons related to patentability. Accordingly, the amendment to claim 1 does not create prosecution history estoppel, and in the event that these claims are allowed and issue, the doctrine of equivalents is available for all the elements of these claims.

Request for Reconsideration of Final Office Action. In view of Applicants' previous amendment and argument, the Examiner has withdrawn certain previous rejections, including all art-based rejections [i.e., rejections under 35 U.S.C. § 112, first paragraph directed to claims 1, 6-7, 9 and 18-20; rejections under 35 U.S.C. § 112, second paragraph directed to claims 1-3, 6-7, 9-12, and 14-21; rejections under 35 U.S.C. 102(b) directed to claims 1-2, 6-7, 10-12, 14-17, 66, and 68-70 (U.S. Patent No. 5,605,798) and claims 1-3, 6-7, 9-12, 14, 17-21, 66, and 69-70 (U.S. Patent No.

5,705,813); and rejections under 35 U.S.C. §103(a) directed to claims 9 and 67-68 (U.S. Pat. Nos. 5,705,813 and 5,716,825)]. A single rejection has been maintained (i.e., the rejection of claim 66 under 35 U.S.C. §112, first paragraph).

As the Examiner will recall, Applicants' previous amendment, mailed November 25, 2002, was made following an interview with the Examiner on November 19, 2002, and an understanding that modification of claim 1 would overcome the cited art. In the present Office Action, which the Examiner has made a Final Office Action, the Examiner cites entirely new art. This is the first opportunity Applicants have had to consider and respond to such new art. Accordingly, Applicants believe that they responded in good faith to the prior art, and should equitably have an opportunity to respond to the newly cited art, which is entirely different from earlier-cited art, free of a final rejection. Accordingly, reconsideration of the Final Office Action is respectfully requested.

The Examiner's Rejection: Specification

The Examiner objects to Applicants' earlier amendment of page 7 (lines 9-19) to the Specification under 35 U.S.C. §132 as introducing new matter into the disclosure of the invention. The Examiner alleges that the addition of the term "ceramic" as a type of substrate is not supported by the original disclosure. The Applicants respectfully call to the Examiner's attention originally filed claims 6, 24 and 49 where "ceramic" is specifically disclosed as a substrate solid phase composition. These originally filed claims all contain the language ".....wherein said substrate is a solid phase composition comprising silicon, glasses, plastics, polymers, metals, ceramics or mixtures thereof." The originally filed claims are part of the disclosure of the invention. Accordingly, Applicants' amendment is supported by the original disclosure and did not introduce new matter. The Applicants respectfully request that the Examiner reconsider and withdraw the rejection under 35 U.S.C. §132, and permit Applicants' amendment to the Specification.

Rejection Under 35 U.S.C §112 (First Paragraph)

Claim 66 stands rejected under 35 U.S.C. §112 (first paragraph) as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors had possession of the claimed invention at the time the application was filed.

Claim 66 recites that the substrate is silicon, semiconductors, insulators, glasses, plastics, polymers, metals, or ceramics. The term "organic materials" was originally included, but was deleted in Applicants' amendment mailed November 25, 2002. The Examiner notes that the specification discloses substrates of glass, metal foil, plastics and silicon wafers (c.f., page 20, lines 5-6), but alleges that the specification does not teach insulators, organic materials, polymers or ceramics as substrates. The question of organic materials is moot in view of Applicants' previous amendment. The Applicants direct the Examiner to page 7, lines 14-16 which reads ".... the substrate supporting these films is composed of a material such as glass, metal, insulation material, plastic material, silicon or semiconductor-containing material." Accordingly, this claim is fully supported in the specification at the time the application was filed. The Applicants respectfully request that the rejection under 35 U.S.C. §112 (first paragraph) be reconsidered and withdrawn.

Claim Rejections Under 35 U.S.C. §102

Claims 1-2, 10, 12, 14 and 69-70 stand rejected under 35 U.S.C. §102(b) as being anticipated by Hutchens *et al.* (U.S. Patent No. 5,719,060). The present invention is not anticipated by Hutchens *et al.*

Hutchens *et al.* may be characterized as an improved MALDI (Matrix Assisted Laser Desorption-Ionization) system. In traditional MALDI, the matrix is a UV-absorbing organic material. As the Examiner notes, this patent utilizes a "matrix" material (i.e., attaching organic molecules to a surface to act as a matrix and analyte affinity material). Hutchens *et al.* notes (col. 4, lines 13-19):

.....the analyte is not dispersed in a matrix solution or crystalline structure but is presented within, on or above an attached surface of energy absorbing "matrix" material through molecular recognition events, in a position where it is accessible and amenable to a wide variety of chemical, physical and biological modification or recognition reactions.

In Hutchens *et al.* the substrate (forming the probe tip or other sample presenting surface) may be derivatized with one or more affinity reagents for selective bonding with predetermined analytes or classes of analytes (c.f., col. 4, lines 38-42). The analyte thus captured by molecular recognition events with "matrix" material, is then desorbed/ionized. In direct contrast to Hutchens *et al.*, the method of Applicants invention applies sample (analyte) directly to a deposited continuous semiconductor or insulator thin film, thereafter analyzing the sample by light desorption-ionization mass spectroscopy, and does NOT utilize any matrix or other material. The use of a continuous semiconductor or insulator thin film without the use of a matrix is a significant element of Applicants' invention and is clearly distinguished from Hutchens *et al.* The absence of matrix material proves distinct advantages over matrix technologies, including, but not limited to, the ability to analyze small molecules by mass spectroscopy, which is not possible with MALDI. The rejection under Hutchens *et al.* should be reconsidered and withdrawn.

Claims 1-3, 10, 12, 14, 17, 66 and 69-70 stand rejected under 35 U.S.C. §102(e) as being anticipated by Nelson *et al.* (U.S. Patent No. 5,955,729). The present invention is not anticipated by Nelson *et al.* It is important to note that Nelson *et al.* is directed to a method of surface plasmon resonance-mass spectrometry in contrast to Applicants' invention which is a method for analyzing a sample by light desorption/ionization mass spectroscopy. The method of Nelson *et al.* involves several steps: capturing an analyte within a sample by means of an interactive surface layer (affixed to a conductive material, including metals like gold and silver), analyzing the analyte by surface plasmon resonanace (involving a first light beam), and thereafter analyzing the captured analyte (involving a second light beam) by desorbtion/ionization

techniques (i.e., fast ion bombardment/ FAB; secondary ion mass spectrometry/SIMS, plasma desorption mass spectrometry, massive cluster impact/MCI, laser desorption/ionization, and matrix-assisted laser desorption/ionization/MALDI, c.f., col. 12, lines 49-67) from the interactive surface area. As the Examiner notes, Nelson *et al.* uses an "interactive surface layer" affixed to a conductive material (including metals). Applicants method is quite different from that of Nelson *et al.*, and certainly does not use surface plasmon resonance. Also, applicants do not use an interactive surface layer to capture an analyte in a sample, but rather apply a sample directly to a deposited continuous semiconductor or insulator thin film. In general, interactive surface layers include hydrogels (i.e., hydrogel of a polysaccharide such as carboxymethylated dextran, c.f., col. 3, lines 64-66).

In addition, while Nelson *et al.* may deliver samples to an interactive analysis (IA) sensor chip surface (i.e., IA analysis is derived entirely from the interaction properties of the ligand on the surface and the analyte in solution) by a fully automated deliver flow system, this IA is an entirely different system from that of Applicants' invention. Nelson *et al.* is clearly distinguished from the present invention. The 35 U.S.C. §102(e) rejection under Nelson *et al.* should be reconsidered and withdrawn.

Claims 1-2, 6-7, 10-12, 14, 17, 66, and 69-70 stand rejected under 35 U.S.C. §102(e) as being anticipated by Siuzdak *et al.* (U.S. Patent No. 6,288,390). The present invention is not anticipated by Siuzdak *et al.* The Examiner notes that Siuzdak *et al.* teaches a method for ionizing an analyte from light absorbing semiconductors (i.e., silicon and germanium) using mass spectrometry. However, Siuzdak *et al.* is limited exclusively to use of porous semiconductor substrate material. This is clearly distinguished from, and in direct contrast to, Applicants' method where sample is applied to deposited continuous semiconductor or insulator thin film material. Siuzdak *et al.* typically uses electrochemical etching to obtain porous material (c.f., col. 20, Example 1). Siuzdak does not teach the use of continuous thin film material for the analysis of sample by light desorption/ionization spectroscopy. Siuzdak *et al.* is clearly

distinguished from the method of the present invention. The 35 U.S.C. §102(e) rejection under Siuzdak *et al.* should be reconsidered and withdrawn.

Claim Rejections under 35 U.S.C. §103

Claims 1-2, 6-7, 10-12, 14, 17-19, 66-67, and 69-70 are rejected under 35 U.S.C. §103(a) as being unpatentable over Siuzdak *et al.* (U.S. Patent No. 6,288,390) in view of Mian *et al.* (U.S. Patent No. 6,319,469). The combination of Siuzdak *et al.* and Mian *et al.* does not arrive at Applicants' invention. This art combination does not disclose the parameters of the claimed process. As discussed above, Siuzdak *et al.* teaches only the use of porous semiconductor substrate material for analyzing an analyte by mass spectroscopy. Siuzdak *et al.* does not teach the use of deposited continuous thin film material, let alone deposited continuous semiconductor or insulator thin film. Prior to Applicants' invention, it was unknown to be able to analyze an analyte directly by mass spectroscopy, preferably light desorption/ionization mass spectroscopy, using deposited continuous semiconductor or insulator thin film material. The teaching of Mian *et al.* is clearly directed to microfluidic systems and the teaching of Siuzdak *et al.* is directed to porous material. These combined references do not either teach or suggest Applicants' claim limitations. It is the Applicants' position that there is no suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify an art reference, or combined references, to arrive at Applicants' invention. The successful use of deposited continuous semiconductor or insulator thin films for sample analysis by light desorption/ionization is unexpected and unprecedented in the art. The cited art, even in combination, does not arrive at Applicants' invention.

Claims 1, and 15-16 are rejected under 35 U.S.C. §103(a) as being unpatentable over Siuzdak *et al.* (U.S. Patent No. 6,288,390) in view of Farmer *et al.* [J. Mass Spectrom., 3:697-704 (1998)]. By the present amendment, Applicants have cancelled claims 15 and 16. Accordingly, this rejection is now moot and should be withdrawn.

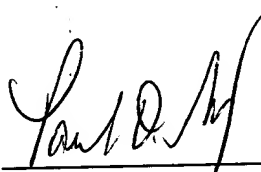
Conclusion

The present invention represents a new and unobvious method for the analysis of a sample by desorption-/ionization mass spectroscopy. The newly amended claim 1 is offered to more particularly point out and distinctly claim the subject matter which Applicants regard as the invention. The amended claim, and dependent claims reading thereon, directed to the method of the invention are believed to define over the art and satisfy statutory conditions of patentability.

In view of the above remarks responsive to the subject Office Action, the Applicants believe that the rejections under 35 U.S.C. §§ 132, 102(b), 102(e), and 103(a) should be withdrawn. The claims as currently presented distinguish from the art references, are fully supported in the specification, and represent patentable subject matter. Reconsideration and allowance, being in order, are earnestly solicited. Should there be further issues, the undersigned would welcome a telephone call to facilitate their resolution.

Respectfully submitted,

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Paul D. Greeley
Attorney for Applicants
Registration No. 31,019
Ohlandt, Greeley, Ruggiero & Perle, LLP
One Landmark Square
Stamford, CT 06901-2682
Tel. (203) 327-4500
Fax. (203) 327-6401

VERSION WITH MARKINGS TO SHOW CHANGES MADE

Claim Summary: Claims 1-65 were originally filed. New claims 66-118 were added by amendment mailed July 15, 2002. Claims 9, 20-65 and 71-118 were cancelled by amendment mailed November 25, 2002. Claims 15 and 16 have been cancelled by the present amendment. Claims 1-3, 6, 7, 10-12, 14, 18-19, 66, 67, 69 and 70 are currently pending and have been examined on the merits in the present Office Action.

In the Claims:

Claims 15 and 16 are cancelled by the present amendment.

The claims have been amended by the present amendment as follows:

1. (Thrice Amended) A method for the analysis of a sample comprising:

(a) applying said sample to a deposited continuous thin film by either adsorption or directly to a surface of said deposited continuous thin film, wherein said deposited thin film is selected from the group consisting of: semiconductors, insulators, and any combinations thereof; and

(b) analyzing said sample by light desorption-/ionization mass spectroscopy.